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PATENT

What is claimed is:

1. An immunogenic composition for administration to a patient mammal having diseased cells, comprising:

(a) an autologous target diseased cell which expresses one or more primary and costimulatory T cell activation molecules at a level higher than said diseased cells in said patient mammal; and

(b) a bridge molecule comprising one or more binding sites for one or more costimulatory molecules on the surface of T cells in said patient mammal, wherein said bridge molecule is attached to said target diseased cell.

2. The composition of claim 1, wherein said bridge molecule further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and said bridge molecule is attached to said target diseased cell at said antigens.

3. The composition of claim 1 which is isolated, enriched or purified.

4. The composition of claim 1, wherein said one or more primary and costimulatory T cell activation molecules are selected from the group consisting of MHC class I, ICAM-1, ICAM-2, VCAM-1, B7-1, and B7-2.

5. The composition of claim 1, wherein said one or more

primary and costimulatory T cell activation molecules are expressed from heterologous nucleic acids introduced into said target diseased cell.

6. The composition of claim 1, wherein said target diseased cell is treated with one or more cytokines *in vitro* to increase the expression of said one or more primary and costimulatory T cell activation molecules.

7. The composition of claim 6, wherein said target diseased cell is treated with IFN-γ, TNF-α, or both.

8. The composition of claim 1, wherein said bridge molecule comprises a binding site for CD28 or 4-1BB on the surface of T cells.

9. The composition of claim 2, wherein said antigens are selected from the group consisting of LDL receptor, gp55, gp95, gp115, gp210, CD44, ICAM-1, ICAM-2, collagen and fibronectin receptor, transferrin receptors, Fc receptor, and cytokine receptors.

10. The composition of claim 1, wherein said bridge molecule is an antibody with specific binding affinity to said one or more costimulatory molecules on the surface of T cells.

11. The composition of claim 2, wherein said bridge

molecule is attached to said one or more antigens on the surface of said target diseased cell by covalent bond.

12. The composition of claim 1, wherein said target diseased cell is a tumor cell.

13. The composition of claim 12, wherein said tumor cell is selected from the group consisting of hepatoma, lung cancer, gastric cancer, colorectal carcinoma, renal carcinoma, head and neck cancers, sarcoma, lymphoma, leukemia, brain tumors, osteosarcoma, blade carcinoma, myeloma, melanoma, breast cancer, prostate cancer, ovarian cancer, and pancreas carcinoma.

14. The composition of claim 1, wherein said target diseased cell is infected with a virus.

15. The composition of claim 14, wherein said virus is selected from the group consisting of HIV, HAV, HBV, HCV, HDV, EBV, HPV, and HLV.

16. An immunogenic composition for administration to a patient mammal having diseased cells, comprising:

(a) an autologous target diseased cell; and

(b) two or more bridge molecules each comprising a binding site for a different costimulatory molecule on the surface of T cells, wherein said bridge molecules are attached

to the surface of said target diseased cell.

17. The immunogenic composition of claim 16 wherein said two or more bridge molecules each comprising a binding site for a different antigen on the surface of said target diseased cell.

18. An immunogenic composition for administration to a patient mammal having diseased cells, comprising:

(a) an autologous target diseased cell; and

(b) a bridge molecule comprising two or more different binding sites for two or more different costimulatory molecules on the surface of T cells, wherein said bridge molecule is attached to the surface of said target diseased cell.

19. The composition of claim 18, wherein said bridge molecule further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and said bridge molecule is attached to said target diseased cell at said antigens.

20. A pharmaceutical composition comprising:

(a) a pharmaceutically effective amount of a cytokine capable of increasing the level of one or more primary and costimulatory T cell activation molecules in tumor cells of a patient mammal;

(b) a pharmaceutically effective amount of a bridge molecule comprising a binding site for an antigen on the surface of said tumor cells and a binding site for a costimulatory molecules on the surface of T cells; and

(c) a pharmaceutically acceptable carrier.

21. A pharmaceutical composition for administration to a patient mammal having diseased cells, comprising:

(a) a pharmaceutically effective amount of an autologous target diseased cell having attached thereto one or more bridge molecules each comprising a binding site for a costimulatory molecule on the surface of T cells in said patient mammal; and

(b) a pharmaceutically acceptable carrier.

22. The composition of claim 21, wherein said one or more bridge molecules each further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and are attached to said target diseased cell at said antigens.

23. A method of preparing an immunogenic composition for administration into a patient mammal having diseased cells, comprising the steps of:

(a) providing an autologous target diseased cell;

(b) treating said target diseased cell to increase the levels of one or more primary and costimulatory T cell

activation molecules;

(c) providing a bridge molecule comprising one or more binding sites for one or more costimulatory molecules on the surface of T cells in said patient mammal; and

(d) attaching said bridge molecule to said target diseased cell;

wherein said steps (c) and (d) are performed either before or after said step (b).

24. The method of claim 23, wherein said bridge molecule further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and said bridge molecule is attached to said target diseased cell at said antigens.

25. The method of claim 23, wherein said one or more primary and costimulatory T cell activation molecules are selected from the group consisting of MHC class I, ICAM-1, ICAM-2, VCAM-1, B7-1, and B7-2.

26. The method of claim 23, wherein said one or more primary and costimulatory T cell activation molecules are expressed from heterologous nucleic acids introduced into said target diseased cell.

27. The method of claim 23, wherein said target diseased cell is treated with one or more cytokines *in vitro* to

increase the expression of said one or more primary and costimulatory T cell activation molecules.

28. The method of claim 27, wherein said target diseased cell is treated with IFN-γ, TNF-α, or both.

29. The method of claim 23, wherein said bridge molecule comprises a binding site for CD28 or 4-1BB on the surface of T cells.

30. The method of claim 24, wherein said antigen is selected from the group consisting of LDL receptor, gp55, gp95, gp115, gp210, CD44, ICAM-1, ICAM-2, collagen and fibronectin receptor, transferrin receptors, Fc receptor, and cytokine receptors.

31. The method of claim 23, wherein said bridge molecule is an antibody with specific binding affinity to said one or more costimulatory molecules on the surface of T cells.

32. The method of claim 24, wherein said bridge molecule is attached to said one or more antigens on the surface of said target diseased cell by covalent bond.

33. A method of curing a patient mammal of diseased cells or reducing growth of diseased cells, comprising the step of administering to said patient mammal a

pharmaceutically effective amount of an immunogenic composition which comprises:

(a) an autologous target diseased cell which expresses one or more primary and costimulatory T cell activation molecules at a level higher than said diseased cells in said patient mammal;

(b) a bridge molecule comprising one or more binding sites for one or more costimulatory molecules on the surface of T cells in said patient mammal, wherein said bridge molecule is attached to said target diseased cell.

34. The method of claim 33, wherein said bridge molecule further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and said bridge molecule is attached to said target diseased cell at said antigens.

35. The method of claim 33 wherein said immunogenic composition is prepared *in vitro*.

36. A method of curing a patient mammal of diseased cells or reducing growth of diseased cells, comprising the steps of:

(a) providing an autologous target diseased cell;

(b) treating said target diseased cell to increase the levels of one or more primary and costimulatory T cell activation molecules in said target diseased cell;

(c) providing a bridge molecule comprising one or more binding sites for one or more costimulatory molecules on the surface of T cells in said patient mammal;

(d) attaching said bridge molecule to said target diseased cell; and

(e) thereafter collecting a pharmaceutically effective amount of said target diseased cell with said bridge molecule attached thereto and administering said collection to said patient mammal;

wherein said steps (c) and (d) are performed either before or after said step (b).

37. The method of claim 36, wherein said bridge molecule further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and said bridge molecule is attached to said target diseased cell at said antigens.

38. The method of claim 36, further comprising the step of removing bridge molecules not attached to said target diseased before step (e).

39. A method of curing a patient mammal of diseased cells or reducing growth of diseased cells, comprising the steps of:

(a) providing an autologous target diseased cell;

(b) providing a bridge molecule comprising a binding site

for a costimulatory molecule on the surface of T cells in said patient mammal;

(c) attaching said bridge molecule to said target diseased cell;

(d) thereafter collecting a pharmaceutically effective amount of said target diseased cell with said bridge molecule attached thereto and administering said collection to said patient mammal; and

(e) administering a pharmaceutically effective amount of one or more cytokines to said patient mammal to increase the levels of one or more primary and costimulatory T-cell activation molecules in said target diseased cell.

40. The method of claim 39, wherein said bridge molecule further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and said bridge molecule is attached to said target diseased cell at said antigens.

41. The method of claim 39, further comprising the step of removing bridge molecules not attached to said target diseased before step (d).

42. A method of curing a patient mammal of diseased cells or reducing growth of diseased cells, comprising the steps of:

(a) providing an autologous target diseased cell;

(b) providing a bridge molecule comprising two or more binding sites for two or more different costimulatory molecules on the surface of T cells in said patient mammal;

(c) attaching said bridge molecule to said target diseased cell; and

(d) thereafter collecting a pharmaceutically effective amount of said target diseased cell with said bridge molecule attached thereto and administering them to said patient mammal.

43. The method of claim 42, wherein said bridge molecule further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and said bridge molecule is attached to said target diseased cell at said antigens.

44. The method of claim 42, further comprising the step of removing bridge molecules not attached to said target diseased before step (d).

45. A method of curing a patient mammal of diseased cells or reducing growth of diseased cells, comprising the steps of:

(a) providing an autologous target diseased cell;

(b) providing two bridge molecules each comprising a binding site for a different costimulatory molecule on the surface of T cells in said patient mammal;

(c) attaching said bridge molecules to said target diseased cell; and

(d) thereafter collecting a pharmaceutically effective amount of said target diseased cell with said bridge molecules attached thereto and administering them to said patient mammal.

46. The method of claim 45, wherein each of said bridge molecules further comprises one or more antigen binding sites for one or more antigens on the surface of said target diseased cell and each of said bridge molecules is attached to said target diseased cell at said antigens.

47. The method of claim 45, further comprising the step of removing bridge molecules not attached to said target diseased before step (d).

48. A bridge molecule for linking a target diseased cell from a patient mammal to an effector cell in said patient mammal, comprising:

(a) a binding site for an antigen on the surface of said target diseased cell; and

(b) two or more binding sites for two or more different costimulatory molecules on the surface of said effector cell.